Claim Rejections – 35 U.S.C. §102(b) As Being Anticipated by *Nilsson, et al.*

Claim 7 (and claims 9-12 which depend therefrom) stand rejected under 35 U.S.C. §102(b) as being anticipated by *Nilsson, et al.* (Science 265:2085-2088, 1994).

The Examiner argues that the oligonucleotide probes disclosed in *Nilsson* for use in the localized detection of specific nucleic acids anticipate the padlock probes that are recited in Applicant's claims. The Examiner further contends that although the claim language "for targeting double stranded nucleic acids," recites an intended method of use, this use cannot be relied upon to distinguish Applicant's claims over the prior art. In particular, the Examiner asserts that the concepts recited in Applicant's composition claims are not germane to the issue of patentability.

Applicant respectfully traverses.

Applicant has amended claim 7 to recite a composition for targeting double stranded nucleic acids, the composition comprising a pharmaceutically acceptable carrier and an effective amount of a padlock probe oligonucleotide having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing with at least substantially neighboring respective regions of a double stranded target nucleic acid so that the padlock probe can be circularized by joining the free end parts to thereby catenate with the target sequence wherein the target sequence is directly inhibited.

As distinguished from Applicant's claims, *Nilsson* neither teaches nor discloses a padlock probe composition in specific combination with an acceptable pharmaceutical carrier. The reference discloses oligonucleotides which are capable of detecting gene sequences, probes which are designed to hybridize to polylinker or oligonucleotide sequences (page 2085), and probes which are directed to the short, nucleotide sequences of human chromosomes (page 2087). The reference, however, fails to teach or disclose probes or oligonucleotide sequences in specific combination with an acceptable

pharmaceutical carrier, as required by the amended claims. Accordingly, *Nilsson* fails to anticipate each and every element of Applicant's invention.

Rejections under 35 U.S.C. § 102(b) dictate that the claimed subject matter be identically disclosed or described in the prior art. Thus, anticipation under 35 U.S.C. § 102(b) requires that all of the material elements recited in a claim be found in a single prior art source. *In re Marshall* (CCPA 1978) 577 F2d 301, 198 USPQ 344. The law is well established that in order to anticipate a claim, the prior art must disclose "each and every element" of the claimed invention. *SSIH Equipment S.A.v. U.S. Inc. Int'l. Trade Commission*, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." (Emphasis added). See also *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 33 USPQ2d 1496 (Fed. Cir. 1995). As discussed herein, *Nilsson* fails to disclose a padlock probe composition in specific combination with an acceptable pharmaceutical carrier, as required by the amended claims. Accordingly, Applicant respectfully requests that the Examiner's rejection under 35 U.S.C. 102(b) of Claim 7 (and claims 8-12 which depend therefrom) be withdrawn.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claim 11 (and claim 12 which depends therefrom) stands rejected under 35 U.S.C. §112, first paragraph as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the invention at the time the application was filed. More particularly, the Examiner argues that the specification provides no examples of the mutually reactive compounds which are recited in claim 11.

Amended claim 11 recites a composition for targeting double stranded nucleic acids wherein the end parts of the composition further comprise mutually chemically reactive compounds.

Applicant respectfully traverses the rejection.

Applicant points out that chemical compounds and functional groups which are capable of joining the end parts of oligonucleotides are well recognized in the art. For Example, *Gryaznov, et al. Nucleic Acids Res*, 22(12):2366-9 (1994) describes the increased selectivity of interactions between oligonucleotide probes and target nucleic acids due to the inclusion of thiophosphoryl and bromoacetamido groups at the respective ends of each oligonucleotide probe, wherein efficient autoligation takes place when the oligonucleotide probes hybridize in a continuous mode to the same complementary strand such that a thiophosphoryl group on one strand and a bromoacetamido group on another strand are brought together into close proximity. Accordingly, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph of amended claim 11 (and amended claim 12 which depends therefrom).

Claim Rejections – 35 U.S.C. §112, Second Paragraph

Claim 11 (and claim 12 which depends therefrom) stands rejected under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter of the invention. More particularly, the Examiner argues that the specification does not adequately define the "mutually reactive compounds" recited in the claims. Applicant reiterates that chemical compounds and functional groups which are capable of joining the end parts of oligonucleotides are well recognized in the art. Accordingly, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §112, second paragraph of amended claim 11 (and amended claim 12 which depends therefrom).

Pending Claims 7-12, As Amended

7. (Amended) A composition for targeting double stranded nucleic acids, said composition comprising a pharmaceutically acceptable carrier and an effective amount of a padlock probe oligonucleotide having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing with at least substantially neighboring respective regions of a double stranded target nucleic acid so that the padlock probe can be circularized by joining said free end parts to thereby catenate with the target sequence wherein said target sequence is directly inhibited.

8. (Cancelled) The composition according to Claim 7 further comprising a pharmaceutical carrier.

9. (Amended) The composition according to Claim 7, further comprising a linking agent, wherein said linking agent is capable of joining said two free nucleic acid end parts.

10. The composition according to Claim 9, wherein said linking agent is a ligase enzyme.

11. (Amended) The composition according to Claim 7, wherein said end parts further comprise a mutually chemically reactive compound.

12. (Amended) The composition according to any one of Claims 7, 9, 10, 11, or 12, wherein said padlock probe comprises a non-natural nucleic acid or polymer.

VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

7. (Amended) A composition for targeting [a] double stranded nucleic acids, [and inhibiting replication thereof, wherein] said composition [comprises] comprising a pharmaceutically acceptable carrier and an effective amount of a padlock probe oligonucleotide having two free nucleic acid end parts which [anneal to two closely adjacent sequences within said double stranded nucleic acid so that the padlock probe is capable of circularization by joining said free end parts and catenating with a target sequence within said double stranded nucleic acid, for inhibition of replication] are at least partially complementary to and capable of hybridizing with at least substantially neighboring respective regions of a double stranded target nucleic acid so that the padlock probe can be circularized by joining said free end parts to thereby catenate with the target sequence wherein said target sequence is directly inhibited.

8. (Cancelled) The composition according to Claim 7 further comprising a pharmaceutical carrier.

9. (Amended) The composition according to Claim [8] 7, further comprising a linking agent, wherein said linking agent is capable of joining said two free nucleic acid end parts.

11. (Amended) The composition according to Claim [8] 7, wherein said end parts further comprise a mutually chemically reactive compound.

12. (Amended) The composition according to any one of Claims [7-11] 7, 9, 10, 11, or 12 wherein said padlock probe comprises a non-natural nucleic acid or polymer.

CONCLUSION

Applicant submits that the amended claims are now in condition for allowance and an early notification of such is solicited.

Respectfully submitted,

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